

CLAIMS

What is claimed is:

5 142. A method of inhibiting fibrosis in a patient said method comprising administering a therapeutically effective amount of somatostatin or a somatostatin agonist to said patient.

143. A method of claim 142, wherein said method comprises administering a therapeutically effective amount of a
10 somatostatin agonist to said patient.

144. A method of claim 143, wherein said fibrosis is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine organ and or in the
15 gastro-intestinal system.

145. A method of claim 143, wherein said fibrosis is induced by chemotherapy, induced by radiation, induced by a drug or a combination of drugs, induced by a disease state, induced by an environmental or an industrial factor, induced by
20 an immune reaction, or induced by a wound.

146. A method of claim 143, wherein said somatostatin agonist is administered parenterally.

147. A method of claim 146, wherein said somatostatin agonist is administered in a sustained release formulation.

25 148. A method of claim 144, wherein said somatostatin agonist is administered parenterally.

149. A method of claim 148, wherein said somatostatin agonist is administered in a sustained release formulation.

30 150. A method of claim 143, wherein said somatostatin agonist is administered topically or orally.

151. A method according to claim 144 wherein the fibrotic disorder in the kidney is glomerulonephritis, diabetic nephropathy, allograft rejection or HIV nephropathy; the fibrotic disorder in the lung is idiopathic fibrosis or

autoimmune fibrosis; the fibrotic disorder in the liver is cirrhosis or veno-occlusive disease; the fibrotic disorder in the skin is systemic sclerosis, keloids, burn scars or eosinophilia-myalgia syndrome and the fibrotic disorder in the
5 central nervous system is intraocular fibrosis.

152. A method according to claim 145 wherein the fibrosis induced by chemotherapy is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine
10 organ or in the gastro-intestinal system.

153. A method according to claim 145 wherein the fibrosis induced by radiation is in the kidney, in the lung, in the liver, in the skin, of the central nervous system, in bone or bone marrow, in the cardiovascular system, in an endocrine
15 organ or in the gastro-intestinal system.

154. A method of inhibiting over-expression of TGF-J which comprises administering to a subject an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

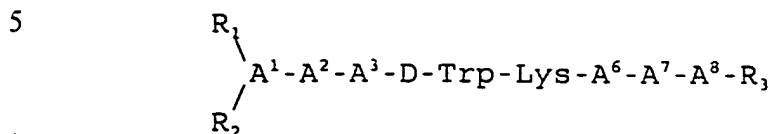
20 155. A method according to claim 154 wherein a somatostatin agonist or a pharmaceutically acceptable salt thereof is administered.

156. A method according to claim 155 wherein the somatostatin agonist has a higher binding affinity for human
25 somatostatin sub-type receptor 1, has a higher binding affinity for human somatostatin sub-type receptor 2, has a higher binding affinity for human somatostatin sub-type receptor 3, has a higher binding affinity for human somatostatin sub-type receptor 4, or has a higher binding affinity for human
30 somatostatin sub-type receptor 5.

157. A method according to claim 155 wherein the somatostatin agonist has a higher binding affinity for two or more of human somatostatin sub-type receptor 1, human somatostatin sub-type receptor 2, human somatostatin sub-type

receptor 3, human somatostatin sub-type receptor 4 or human somatostatin sub-type receptor 5.

158. A method according to claim 155 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, J-Nal, J-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 ,
15 or NO_2 ;

A^2 is Ala, Leu, Ile, Val, Nle, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

A^3 is pyridyl-Ala, Trp, Phe, J-Nal, 2,4-dichloro-Phe,
20 pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A^7 is Ala, Leu, Ile, Val, Nle, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe,
25 wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

A^8 is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, J-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

30 each R_1 and R_2 , independently, is H, lower acyl or lower alkyl; and R_3 is OH or NH_2 ; provided that at least one of A^1 and A^8 and one of A^2 and A^7 must be an aromatic amino acid; and further provided that A^1 , A^2 , A^7 and A^8 cannot all be aromatic amino acids.

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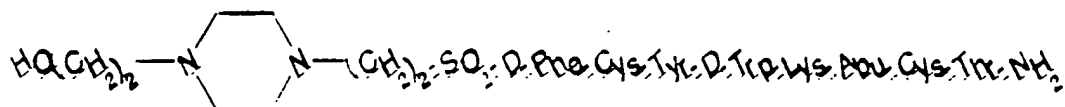
159. A method according to claim 155 wherein the somatostatin agonist is

- H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂;
H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;
5 H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;
H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂;
H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;
H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;
H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-J-D-Nal-NH₂;
10 D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-b-Nal-NH₂;
D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-b-Nal-NH₂;
D-b-Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH₂;
D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH₂;
15 D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;
D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;
Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;
Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
20 H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
25 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Ac-D-Phe-Lys^{*}-Tyr-D-Trp-Lys-Val-Asp-Thr-NH₂, wherein an amide
bridge is between Lys^{*} and Asp;
Ac-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
30 Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-L-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;

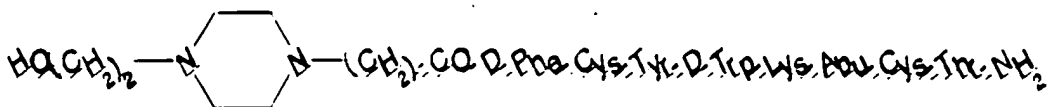
- Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
 Ac-L-hArg(CH₂-CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 5 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH₂;
 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;
 Ac-hArg(CH₃, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 H-hArg(hexyl)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
 10 Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
 Propionyl-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH₂;
 Ac-D-J-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)₂-NH₂;
 Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 15 Ac-D-hArg(CH₂CF₃)₂-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 Ac-D-hArg(CH₂CF₃)₂-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
 Ac-D-hArg(Et)₂-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 20 NH₂;
 Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH₂;
 Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
 Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH₂;
 25 Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH₂;
 Bmp-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH₂;
 H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
 H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
 H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-b-Nal-NH₂;
 30 H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
 Ac-D-b-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH₂;
 H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH₂;
 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH₂;
 H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;

- H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
H-D-Phe-Cys-b-Nal-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH₂;
- 5 cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe) ;
cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe) ;
- 10 cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe) ;
cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe) ;
cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe) ;
- 15 cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe) ;
cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe) ;
cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe) ;
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe) ;
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr) ;
- 20 cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe) ;
cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe) ;
- 25 cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba) ;
cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe) ;
- 30 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH₂)₄CO) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-b-Ala) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe) ;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly) ;

- cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly) ;
 cyclo (Asn-Phe-Phe-D-Trp(F) -Lys-Thr-Phe-Gaba) ;
 cyclo (Asn-Phe-Phe-D-Trp(NO₂) -Lys-Thr-Phe-Gaba) ;
 5 cyclo (Asn-Phe-Phe-Trp(Br) -Lys-Thr-Phe-Gaba) ;
 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I) -Gaba) ;
 cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But) -Gaba) ;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
 10 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys) -OH;
 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys) -
 OH;
 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba) ;
 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba) ;
 15 cyclo (Phe-Phe-D-Trp(5F) -Lys-Thr-Phe-Phe-Gaba) ;
 cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac) -Thr-Phe-NH-(CH₂)₃-CO) ;
 cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
 cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
 cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
 20 D-b-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂;
 H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂;



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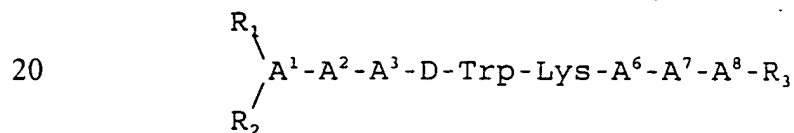


- 30 or D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys) -Thr-ol; or
 a pharmaceutically acceptable salt thereof.

160. A method according to claim 143 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1, has a higher binding affinity for human somatostatin sub-type receptor 2, has a higher
5 binding affinity for human somatostatin sub-type receptor 3, has a higher binding affinity for human somatostatin sub-type receptor 4, or has a higher binding affinity for human somatostatin sub-type receptor 5.

161. A method according to claim 143 wherein the
10 somatostatin agonist has a higher binding affinity for two or more of human somatostatin sub-type receptor 1, human somatostatin sub-type receptor 2, human somatostatin sub-type receptor 3, human somatostatin sub-type receptor 4 or human somatostatin sub-type receptor 5.

15 162. A method according to claim 143 wherein the somatostatin agonist is



or a pharmaceutically acceptable salt thereof, wherein

25 A^1 is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, b-Nal, b-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

A^2 is Ala, Leu, Ile, Val, Nle, Phe, b-Nal, pyridyl-Ala,
30 Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

A^3 is pyridyl-Ala, Trp, Phe, b-Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH_3 , Cl, Br, F, OH, OCH_3 or NO_2 ;

35 A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A^7 is Ala, Leu, Ile, Val, Nle, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe,

wherein X is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

A⁸ is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, b-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

each R₁ and R₂, independently, is H, lower acyl or lower alkyl; and R₃ is OH or NH₂; provided that at least one of A¹ and A⁸ and one of A² and A⁷ must be an aromatic amino acid; and further provided that A¹, A², A⁷ and A⁸ cannot all be aromatic amino acids.

163. A method according to claim 143 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

15 H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-b-D-Nal-NH₂;

20 D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-b-Nal-NH₂;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-b-Nal-NH₂;

D-b-Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;

D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH₂;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH₂;

25 D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;

Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;

30 H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;

H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;

H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;

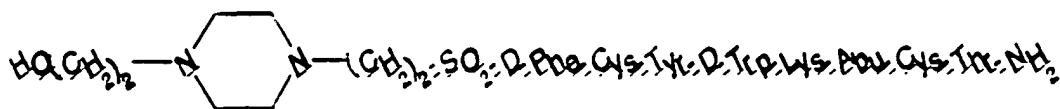
H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;

H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;

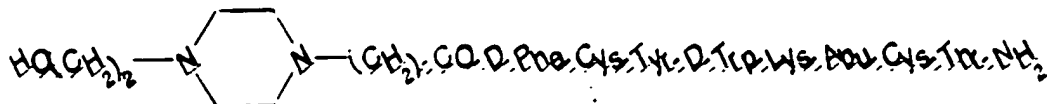
- H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Ac-D-Phe-Lys'-Tyr-D-Trp-Lys-Val-Asp-Thr-NH₂, wherein an amide bridge is between Lys' and Asp;
- 5 Ac-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-L-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
- 10 Ac-D-hArg(CH₂CF₃)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHET;
Ac-L-hArg(CH₂-CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
- 15 Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHET;
Ac-hArg(CH₃, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-hArg(hexyl)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHET;
- 20 Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
Propionyl-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH₂;
Ac-D-J-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)₂-NH₂;
Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
- 25 Ac-D-hArg(CH₂CF₃)₂-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂;
Ac-D-hArg(CH₂CF₃)₂-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂;
Ac-D-hArg(Et)₂-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-
- 30 NH₂;
Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH₂;
Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH₂;

- Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH₂;
Bmp-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH₂;
H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
5 H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-b-Nal-NH₂;
H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂;
Ac-D-b-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-b-Nal-NH₂;
10 H-D-b-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂;
H-D-Phe-Cys-b-Nal-D-Trp-Lys-Val-Cys-Thr-NH₂;
H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH₂;
15 cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe) ;
cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe) ;
20 cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe) ;
cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe) ;
cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-Lys-Ser-Phe) ;
25 cyclo (Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe) ;
cyclo (D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe) ;
cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe) ;
cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe) ;
cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr) ;
30 cyclo (Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe) ;
cyclo (Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe) ;
cyclo (Pro-Tyr-D-Trp-4-Amphe-Thr-Phe) ;

- cyclo (Pro-Phe-D-Trp-4-Amphe-Thr-Phe) ;
cyclo (N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba) ;
5 cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH₂)₄CO) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-b-Ala) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu) -OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe) ;
10 cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gly) ;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly) ;
cyclo (Asn-Phe-Phe-D-Trp(F) -Lys-Thr-Phe-Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp(NO₂) -Lys-Thr-Phe-Gaba) ;
15 cyclo (Asn-Phe-Phe-Trp(Br) -Lys-Thr-Phe-Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I) -Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But) -Gaba) ;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
20 cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys) -OH;
cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys) -
OH;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba) ;
cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba) ;
25 cyclo (Phe-Phe-D-Trp(5F) -Lys-Thr-Phe-Phe-Gaba) ;
cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac) -Thr-Phe-NH-(CH₂)₃-CO) ;
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) ;
30 D-b-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂;
H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂;



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or D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol; or
10 a pharmaceutically acceptable salt thereof.

164. A method according to claim 145 wherein the fibrosis
induced by a drug or a combination of drugs is in the kidney,
in the lung, in the liver, in the skin, of the central nervous
system, in bone or bone marrow, in the cardiovascular system,
15 in an endocrine organ, or in the gastro-intestinal system.

165. A method according to claim 145 wherein the fibrosis
induced by a disease state is in the kidney, in the lung, in
the liver, in the skin, of the central nervous system, in bone
or bone marrow, in the cardiovascular system, in an endocrine
20 organ, or in the gastro-intestinal system.

166. A method according to claim 145 wherein the fibrosis
induced by an environmental or an industrial factor is in the
kidney, in the lung, in the liver, in the skin, of the central
nervous system, in bone or bone marrow, in the cardiovascular
25 system, in an endocrine organ, or in the gastro-intestinal
system.

167. A method according to claim 145 wherein the fibrosis
induced by an immune reaction is in the kidney, in the lung, in
the liver, in the skin of the central nervous system, in bone
30 or bone marrow, in the cardiovascular system, in an endocrine
organ, in the gastro-intestinal system.

168. A method according to claim 145 wherein the fibrosis
induced by a wound is in the kidney, in the lung, in the liver,
in the skin, of the central nervous system, in bone or bone

marrow, in the cardiovascular system, in an endocrine organ, or in the gastrointestinal system.

169. A pharmaceutical composition useful for inhibiting fibrosis in a patient which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

170. A pharmaceutical composition according to claim 169 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.

171. A pharmaceutical composition useful for inhibiting overexpression of TGF-J which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin or a somatostatin agonist, or a pharmaceutically acceptable salt thereof.

172. A pharmaceutical composition according to claim 171 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.

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